L4: Entry 21 of 22 File: JPAB May 30, 1991

PUB-NO: JP403127622A
DOCUMENT-IDENTIFIER: JP 03127622 A
TITLE: PH SENSITIVE LIPOSOME

PUBN-DATE: May 30, 1991

INVENTOR-INFORMATION:

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INT-CL (IPC): B01J 13/02

ABSTRACT:

PURPOSE: To obtain the pH sensitive liposome which increases the fusion rate on an acid side by incorporating specific ratios of phosphatidyl ethanol amine and phosphatidinic acid and/or phosphatidylcerine as film constituting lipid components into this liposome.

CONSTITUTION: The compsn. of the film constituting limpid component consists of the phosphatidyl ethanol amine (the amine derived from natural materials, such as the yoke of eggs or synthesized and semi-synthesized amines are used) and ≤20mol% phosphatidinic acid and/or phosphatidylcerine. The molar ratio of the phosphatidyl ethanol amine and the phosphatidinic acid and/or phosphatidylcerine is 32:1 to 16 and up the about 50% of the phosphatidyl ethanol amine can be substd. with cholesterol. The material for sealing the liposome is exemplified by drugs, nucleic acid, and the analogous matter, thereof, protein, carcinostatic agents, etc. The pH sensitive liposome which increases the fusion rate on the acid side is obtd. in this way.

L4: Entry 19 of 22 File: USPT Feb 1, 1994

DOCUMENT-IDENTIFIER: US 5283122 A
TITLE: Fused liposome and acid induced method for liposome fusion

Abstract Text (1):
Liposomes containing phosphatidylethanolamine, palmitoyl homocysteine or oleic acid or palmitic acid, fuse rapidly when the pH of the medium is reduced below 7. Liposome fusion was measured by (a) mixing of the liposomal lipids as shown by resonance energy transfer, (b) gel filtration and (c) electron microscopy. The presence of phosphatidylethanolamine or acid addition esters thereof in the liposomes greatly enhances fusion; whereas the presence of phosphatidylcholine inhibits fusion. During fusion of liposomes containing phosphatidylethanolamine:palmitoyl homocysteine (8:2), almost all of the encapsulated calcein is released. Inclusion of cholesterol (40%) in the liposomes substantially decreases leakage without impairing fusion. Those pH sensitive liposomes are fused to deliver biologically active molecules such as DNA, into living cells.

Detailed Description Text (23):
The liposomes formed by the method of the present invention will provide an effective cytoplasmic delivery system by fusing with the endosome membranes. The less leaky liposomes containing cholesterol will be particularly useful in discharging their contents into the cytoplasm. For example, foreign material such as drugs, enzymes, hormones, nutrients, antigens, antibodies (monoclonal or conventional), RNA, DNA (natural or recombinant) or any combinations of these and like substances, may be encapsulated in the pH sensitive liposomes of the present invention and ultimately be inserted into a living cell.

L4: Entry 16 of 22 File: USPT May 19, 1998

DOCUMENT-IDENTIFIER: US 5753263 A
TITLE: Method to deliver compositions conferring resistance to alopecia to hair follicles

Brief Summary Text (34):
A liposome composition can comprise any of a variety of liposomes designed to selectively target hair follicles, including pH-sensitive liposomes, liposomes comprising a phospholipid selected from the group consisting of phosphatidylcholine (PC), egg phosphatidylcholine (EPC), dioleoylphosphatidylcholine (DOPC), dipalmitoylphosphatidyl choline (DPPC), phosphatidylethanolamine (PE), dioleoylphosphatidylethanolamine (DOPE) and cholesterol, liposomes further comprising a cationic phospholipid selected from the group consisting of D282, D378, D383, D3886, D3897 and D3899, (obtainable from Molecular Probes Catalog, Eugene, Oreg.) and the like formulations.

Detailed Description Text (65):
In another embodiment, the invention comprises a liposome composition comprising one or more phospholipids selected from the group consisting of PC, EPC, DOPC, DPPC, PE, DOPE and cholesterol, combined with one or more phospholipids to form pH-sensitive liposomes. pH-sensitive liposomes are generally well known and their preparation has been described by Straubinger et al., FEBS Letts. 179:148-154, 1985. A preferred pH sensitive liposome comprises oleic acid (OA) and PE at a molar ratio of 3:7. OA is available from a variety of commercial sources, including Sigma (St. Louis, Mo.). Several pH-sensitive liposome systems have been described. There are two main categories: intrinsically pH-sensitive liposomes and those which utilize an external non-lipid trigger. Intrinsically pH-sensitive liposomes are constructed by combining phosphatidylethnolamine (PE) with one of a number of acidic amphiphiles. Externally triggered pH-sensitive liposomes combine an otherwise stable liposome with an external soluble component such as a titratable polymer or a titratable synthetic peptide which undergoes a conformational change upon acidification. To increase the efficacy of intracellular delivery, liposomes can be made pH-sensitive and able to fuse with cellular membrane at decreased pH values (pH drop from 7.4 to 6.5) or in the presence of polyethylene glycol. Some pH-sensitive liposomes are composed of DOPE:Cholesterol hemisuccinate at molar ratios 2:1.